

REMARKS**Overview**

Claims 66-69 and 71-83 are pending in this application. Claims 79-83 are new. Claim 66 has been amended.

Issues Under 35 U.S.C. § 112

Claims 66-69, 71-78 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention. The Applicant respectfully traverses.

One skilled in the art would recognize that the phrase "distal to a thrombus site" was disclosed in the specification as originally filed. As the Examiner correctly points out, on page 2 of the Office Action, the specification describes the use of microbubbles to relieve thrombus obstruction; however, the Examiner is incorrect in concluding that there is no specific teaching about relieving trauma associated with the obstruction of vessels distal to thrombus site. The originally filed specification is laden with ample examples of bubbles introduced into the vessels which then travel to the thrombus site or downward of the thrombus to prevent trauma from an embolus occluding a vessel distant from the original site. While the Examiner is correct that nowhere in the application is the word "distal" used, the specification reasonably conveys to one skilled in the art that it applies to vessels which are distal, "distant" (originally filed specification, page 2, line 5), or away from the thrombus site. These phrases are all analogous and Applicant invites the Examiner to enter an Examiner's amendment replacing "distal" with "distant" or "away from" if the Examiner so chooses.

The word "distal" means "anatomically located far from the origin" (The American Heritage Dictionary, second college edition, 1982). One of ordinary skill in the art would recognize that distal in the set of the claims are located far from the thrombus site, distant from the thrombus site, or away from the thrombus site. This conclusion is justified as the original file specification teaches that it is the "insoluble gas microspheres of the invention (that) act themselves as a thrombolytic agent" (specification, page 5, Summary of the Invention, lines 13-15). In addition, there is ample support of the premise that the microbubbles are activated by sonication away from the thrombus site as the pharmaceutical liquid is injected into the animal and then transmitted in the vessels to the thrombus site (page 11, last paragraph, line 7) and then ultrasound applied to the vessels such that "the ultrasound signal activates the microbubbles so that the microbubbles themselves as a thrombolytic agent" (page 12, lines 5-8).

Finally, there is specific teaching about relieving trauma associated with the obstruction of vessels distant to the thrombus site as the specification clearly includes teaching that "the thrombus can become an embolus and occlude a vessel distant from the original site" (specification, page 2, lines 4-6).

Accordingly, the Applicant respectfully requests the Examiner withdrawn the objection to claims 66-69, 71-78 as incorporating new matter.

Issues Under 35 U.S.C. § 102

Claims 66-69, 71, 75-78 were rejected under 35 U.S.C. § 102(b) as being anticipated by Tachibana et al U. S. Patent No. 5,315,998 (Tachibana) or Feinstein U. S. Patent No. 4,718,433 (Feinstein). Claim 66 has been amended to include the limitation "applying ultrasound to the vessels in the area of trauma, distal to the thrombus site". Neither Tachibana nor Feinstein teach applying ultrasound to the vessels in the area of trauma that are distant or away from the

thrombus site. Moreover, the Applicant has amended the preamble to modify pending claim 66 to require "without thrombus dissolution and recanalization" as guided by the Examiner from page 4 of the Office Action, lines 10-13. This "without" limitation is relevant as the Applicant teaches the steps to relieve trauma without directly dissolving the thrombus while testing vessels distant from the thrombus site. Finally, the Applicant has clarified the meaning of "distal to the thrombus site" in this amendment and also indicated that the ultrasound is to be applied to "vessels in the area of trauma".

The Applicant respectfully requests the Examiner to withdraw the 102 rejection as neither Tachibana nor Feinstein meet the limitation of "applying ultrasound to the vessels in the area trauma, distal of thrombus site" or teach "increasing blood flow with thrombus dissolution and recanalization in animals". As claims 67-69, 71, and 75-78 depend from claim 66, it is respectfully requested that this rejection be withdrawn with regard to these claims as well.

Issues Under 35 U.S.C. § 103

Claims 66-69, 71 and 75-78 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Siegel U. S. Patent No. 5,695,460 (Siegel) in view of Tachibana, Feinstein and further in view of Schutt U. S. Patent No. 5,605,673 (Schutt). Siegel does not teach "applying ultrasound to the vessels in the area of trauma, distal to the thrombus site". Accordingly, Siegel does not teach the limitation of claim 66 as amended. Similarly, Schutt does not teach the limitation of "applying ultrasound to the vessels in the area of trauma, distal to the thrombus site". Therefore, the Examiner should withdraw this rejection as it would not have been obvious to one of ordinary skill in the art at the time of the invention to apply ultrasound to the "vessels in the area of trauma" to relieve trauma by increasing blood flow with thrombus dissolution and recanalization in animals through the combination of Siegel in view of Tachibana, Feinstein and Schutt.

New Claims

Claim 79 is a new independent claim that includes the limitation "applying ultrasound to the pharmaceutical composition following intravenous injection and during transit to the thrombus". This limitation is supported on page 11, last paragraph, and page 12, lines 5-7. The prior art does not teach applying ultrasound to the pharmaceutical composition outside of being within the thrombus. The Applicant's invention recognizes that it is the microbubbles that dissolve the thrombus as apposed to the microbubbles being formed by ultrasound energy within the thrombus. The Applicant's invention clearly recognizes that microbubbles may be formed by ultrasonic energy inside the vessels and during transit to the thrombus site. Accordingly, claim 79 should be found allowable. As claims 80 and 81 depend from claim 79, these should be found allowable as well.

New claim 82 is a method claim for "relieving trauma associated with destruction of vessels close to a thrombus site". Claim 82 has the limiting step "applying ultrasound to the vessels in the area of trauma, close to and not on the thrombus site." Support for this amendment and negative limitation is found in the original filed specification in which states "generally the pharmaceutical liquid composition is injected into the area of the thrombus or close thereto and then ultrasound is applied" (page 11, lines 10-13). Therefore, the Applicant teaches to one skilled in the art that ultrasound may be applied close to a thrombus and not directly upon the thrombus. Prior art teaches nothing of the sort but instead teaches applying ultrasound directly to the thrombus.

Further support for this limitation may be found in the original filed specification stating that the microbubbles are injected "near the side of the thrombus" (page 13, lines 1-2). In addition, the specification discloses "generally the pharmaceutical liquid composition is injected

into the area of the thrombus or close thereto and that ultrasound is applied" (page 16, Gas Perfusion of Samples section, lines 5-8). Accordingly, one skilled in the art would recognize that ultrasound may be applied close to the area of the thrombus but yet isolated from the thrombus.

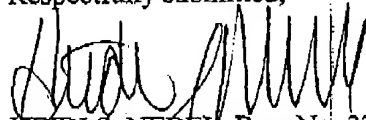
Therefore, the Applicant respectfully requests allowance of claims 79-82.

Conclusion

This is a request under the provision of 37 CFR § 1.136(a) to extend the period for filing a response in the above-identified application for one month from June 9, 2004 to July 9, 2004. Applicant is a small entity; therefore, please charge Deposit Account number 26-0084 in the amount of \$55.00 for one month to cover the cost of the extension. Any deficiency or overpayment should be charged or credited to Deposit Account 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,



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